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ALTERED GRAVITY AS A TOOL FOR TISSUE ENGINEERING: IMPLICATIONS ON PROLIFERATION AND DIFFERENTIATION OF A NEURONAL MODEL

Abstract

A large number of evidences in the literature has shown that altered gravity can represent an effective physical stimulus for the achievement of several tissue constructs in vitro starting from cell suspensions. Microgravity conditions have been largely applied for the study of responses of several kinds of cells. For instance, it was used to obtain human pancreatic carcinoma constructs recapitulating tumor complexity in vitro (Nakamura 2002), and to arrange human mesenchimal stem cell into spheroids showing an enhanced osteogenic differentiation (Cerwinka 2012). Simulated microgravity was also tested with PC12 adrenal medullary cells to explore the possibility of obtaining neuroendrocrine organoids (Lelkes 1998). Derived from a rat pheochromocytoma, PC12 cells in fact mimic many characteristics of dopaminergic neurons, and reversibly express a sympathetic phenotype upon administration of nerve growth factor. They represent an established neuronal model and even a valuable source for xenotransplants. In the presence of microgravity conditions, PC12 cell neuroendocrine differentiation was shown to be enhanced by increase of a catecholaminergic enzyme expression (phenylethanolamine-N-methyltransferase). The application of hypergravity regimes has been instead relatively unexplored for tissue culture purposes. In a previous work by the Authors (Ciofani 2012), C2C12 myoblast proliferation and differentiation were shown to be increased by hypergravity treatment. In this study, we hypothesized that hypergravity might also affect PC12 cell behavior. To test this, we applied hypergravity stimulation for 1h with different acceleration values, utilizing in particular different protocols for differentiating cultures. We performed several qualitative and quantitative analyses (fluorescent stainings, metabolism assay, gene expression analysis) and we found that proliferation was slightly increased, whereas differentiation was more markedly enhanced by higher acceleration values. Although preliminary, our results suggest that hypergravity might induce a faster and better cellular differentiation, and encourage further investigations concerning the potential of hypergravity treatments to the achievement of cellular constructs for the therapy several neural disorders.

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Lelkes et al, In Vitro Cellular and Developmental Biology- Animal 3l4: 316-325 (1998)
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